



Impact of a 14-3-3 Protein on the Smooth Muscle Contractility in *C. elegans*

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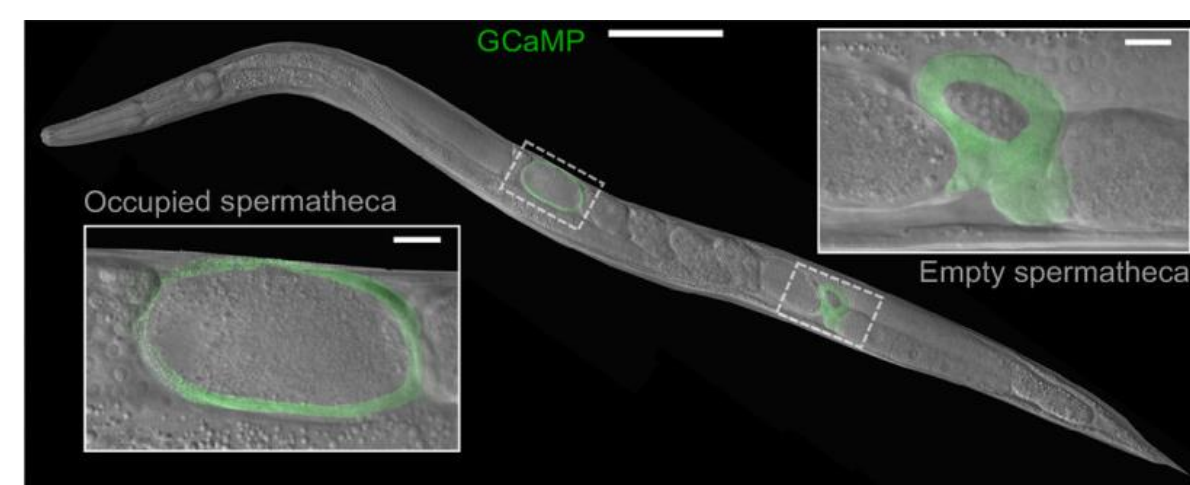


Abstract

Contraction of smooth muscle is one of many systems that enable organisms to coordinate their responses to mechanical stimuli. Dysregulation in smooth muscle contraction can lead to conditions such as asthma, hypertension, and GI disorders in humans. Using *C. elegans* to model smooth muscle contractility, we examine possible regulators of the 14-3-3 adapter protein, *ftt-2*, by systematically knocking down regulating genes with human homologs.

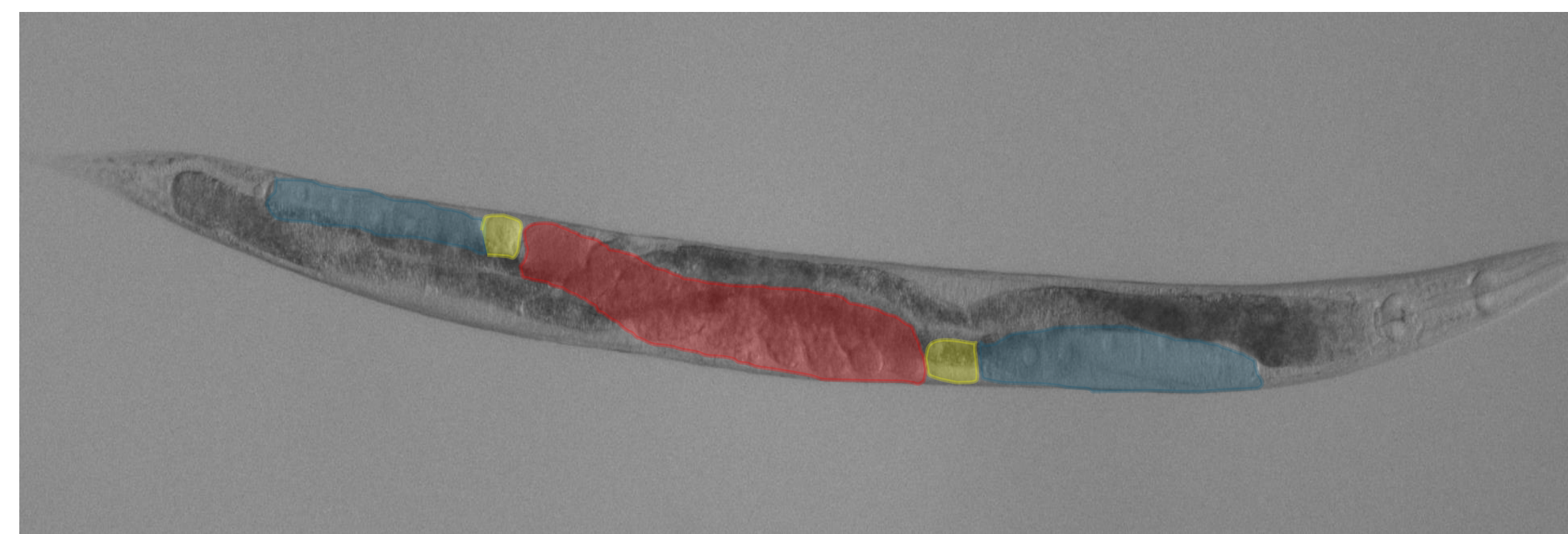
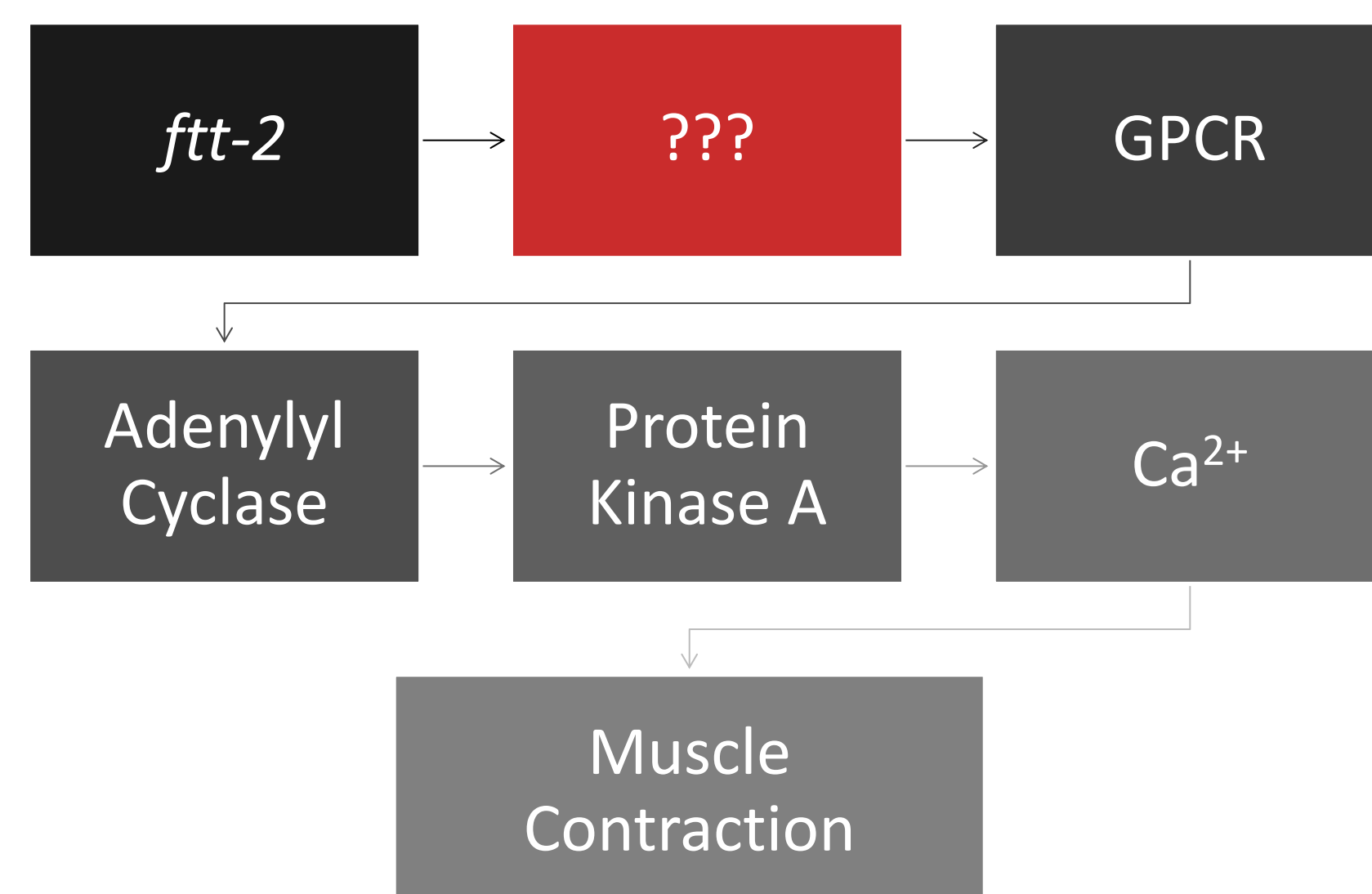
Background

In *C. elegans*, embryo fertilization occurs in an organ called a spermatheca, a tube-like structure positioned between the ovaries and uterus. In *C. elegans* lacking *ftt-2*, over 50% of embryos are not passed through to the uterus, resulting in fertilized eggs being trapped, "occupying" the spermatheca.



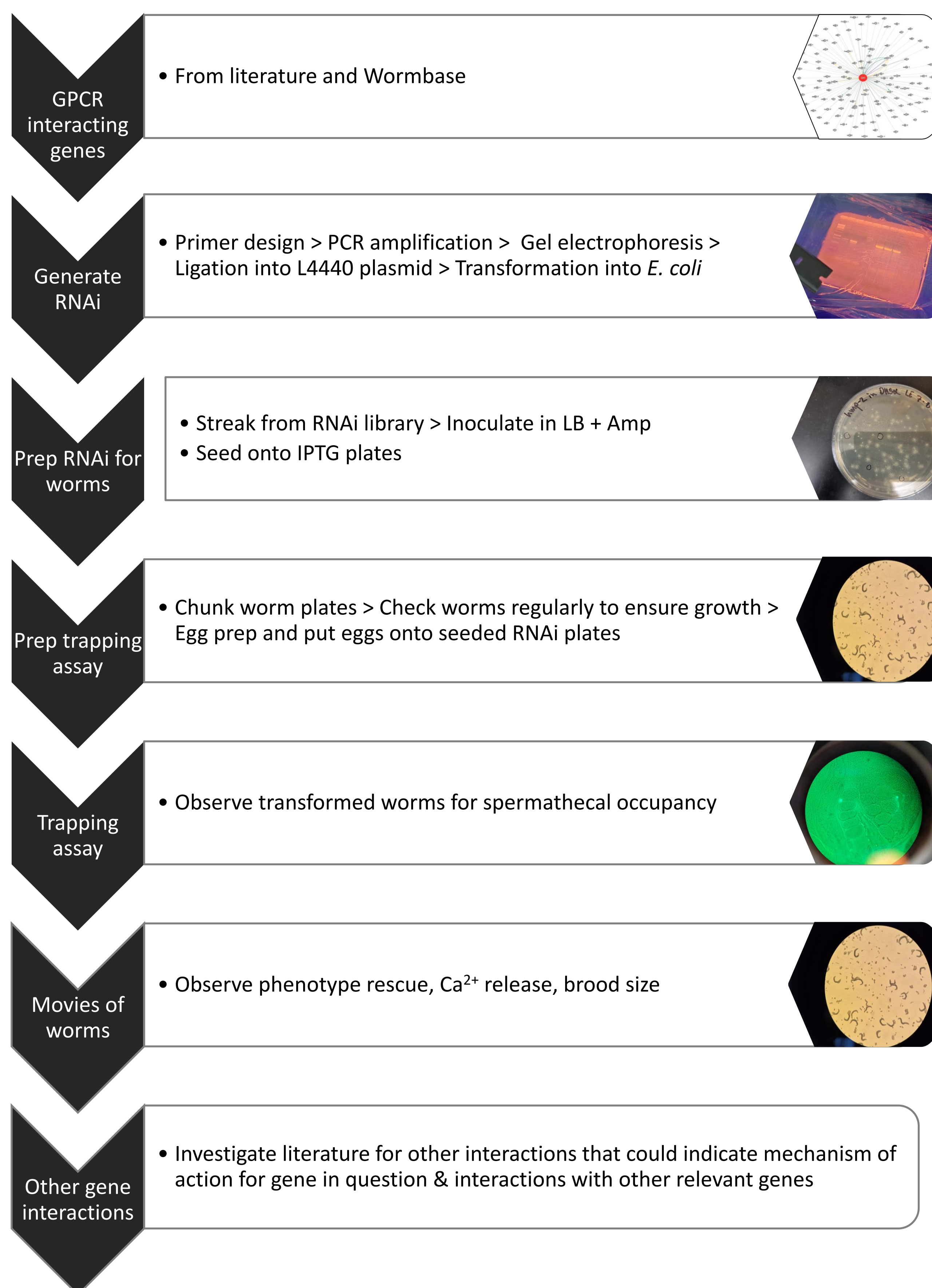
Ca²⁺, which acts as a messenger to stimulate cell contraction, was observed to be released at higher levels in spermathecae of *ftt-2* lacking worms than in wild type, even during normally quiescent periods.

Variation in Ca²⁺ release in conjunction with high rates of occupied spermatheca suggests that the change in phenotype is caused upstream of Ca²⁺ release, implicating GPCRs at the beginning of the Ca²⁺ pathway. By targeting GPCR-interacting genes, we aim to elucidate how *ftt-2* impacts contractility by using a suppressor screen to identify genes which could be overexpressed without FTT-2 maintaining normal cell function.



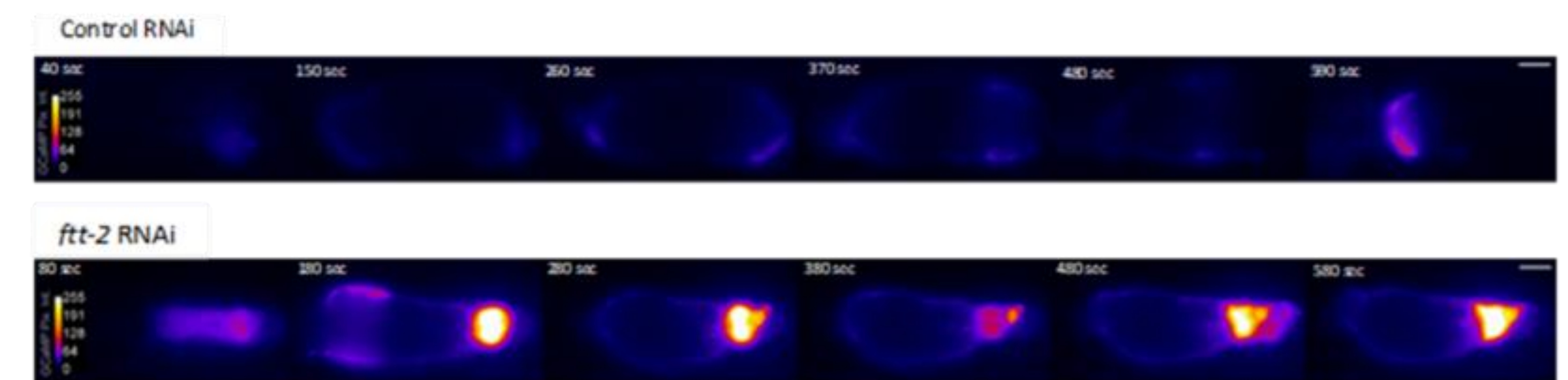
- Gonad arm: Developing oocytes
- Spermatheca: Sperm storage and site of fertilization
- Uterus: Fertilized eggs

Materials & Methods

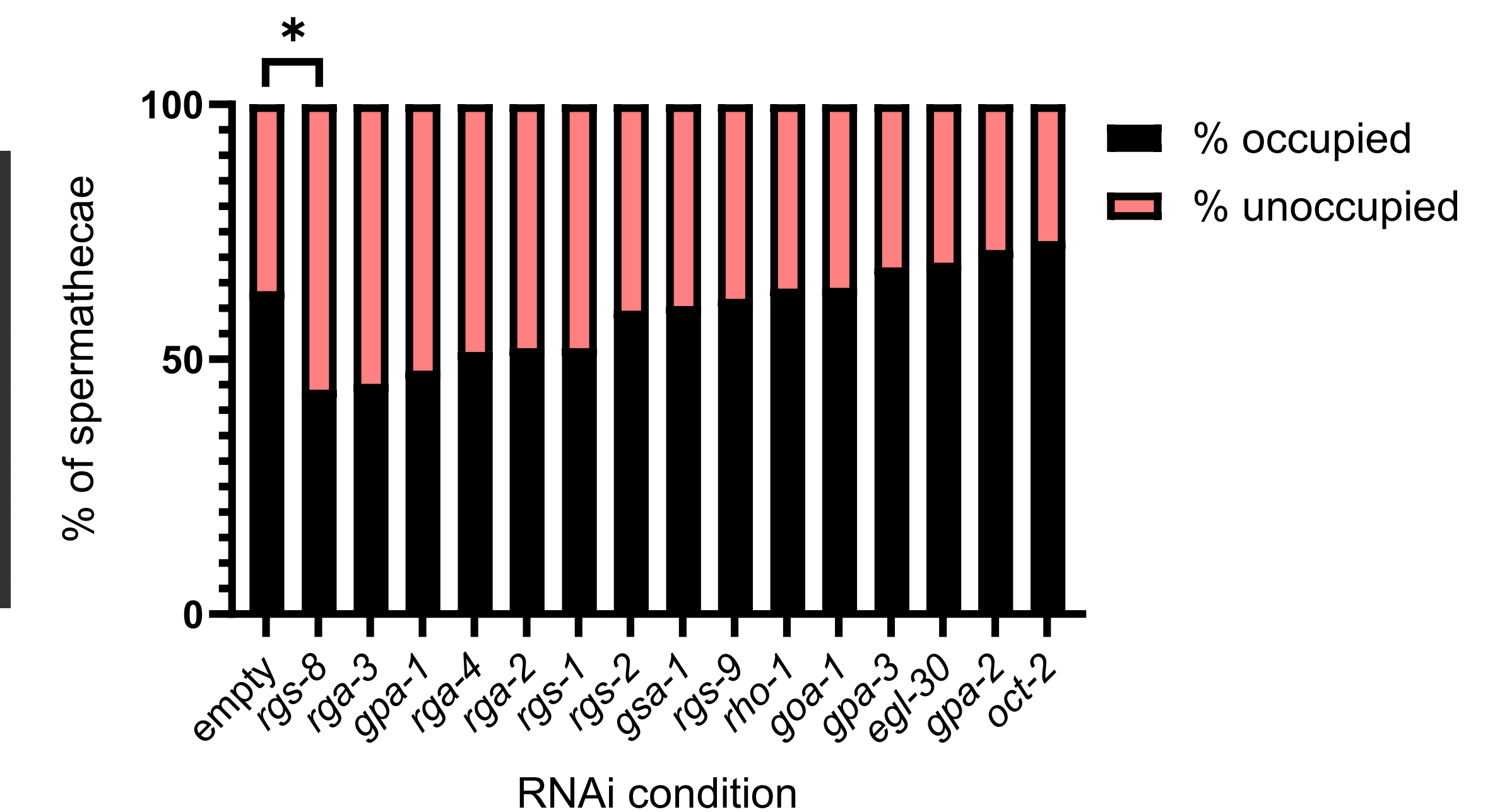
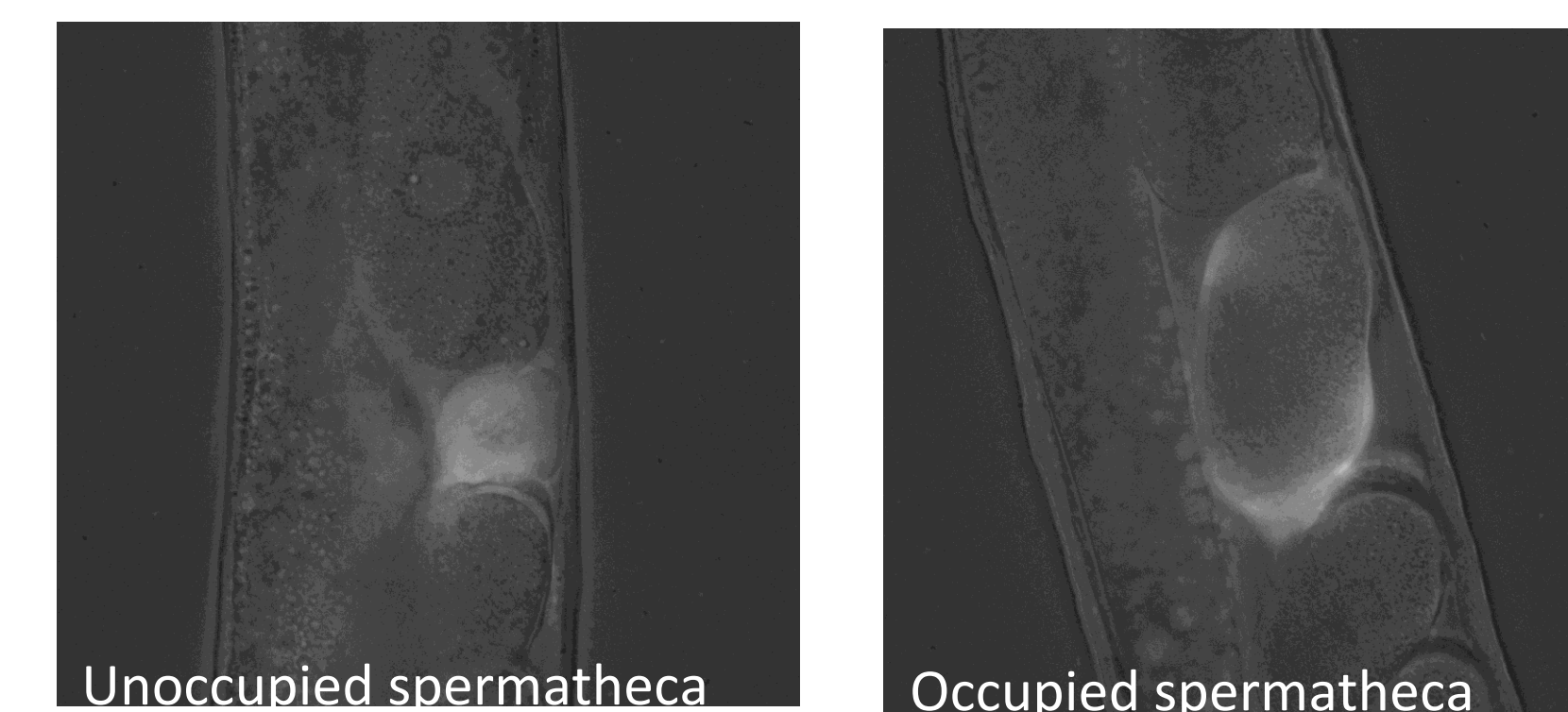


Results

Lack of FTT-2 in the spermatheca causes more calcium to be released, making the spermathecal valve very squeezey, resulting in more trapped oocytes.



Of the GPCR-interacting genes examined in this experiment, only *rgs-8* has a statistically significant impact on the occupancy of the spermatheca.



Discussion

rgs-8 is an ortholog of the gene *rgs-1*, which regulates the activity of the G-protein alpha subunit binding. The correlation between the knockdown of *rgs-8* and reduced spermathecal occupancy provides evidence that *rgs-8* could act to inhibit *ftt-2* or stimulate Ca²⁺ release in the spermatheca.

Next steps include investigating the effects of *rgs-8* knockdown in *ftt-2* mutant worms :

- Time-lapse imaging of the spermathecal Ca²⁺ release
- Confocal imaging of the spermathecal cytoskeleton

We will also continue to examine the list of possible FTT-2 interactors.

References

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